ENHANCED COMPOSITION FOR TREATMENT OF OBESITY

RELATED APPLICATIONS

This application is filed as a continuation-in-part patent application filed under 37 CFR 1.53(b)(2) of patent application number 09/732,137, filed on December 7, 2000 titled "Composition for Treatment of Obesity," which was a continuation-in-part application of application number 09/629,578, filed on July 31, 2000, titled "Composition and Method for Treatment of Gastrointestinal Disorders, Hyperlipidemia and Autoimmune Diseases," invented by Gregory G. Bojrab.

BACKGROUND

Field of the Invention

The present invention relates to the field of treatment of gastrointestinal disorders, hyperlipidemia, autoimmune diseases and obesity. More particularly, the present invention relates to a probiotic composition, and a method for treatment of obesity using the composition.

Background of the Invention

Gastrointestinal disease includes many disorders, including but not limited to, inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, infectious enteritis (viral, bacterial, parasitic), antibiotic associative diarrhea, clostridium difficile colitis,

microscopic or lymphocytic colitis, collagenous colitis, colon polyps and familial polyp syndromes (e.g., familial polyposis syndrome, Gardner's Syndrome), helicobacter pylori, irritable bowel syndrome, nonspecific diarrheal illnesses, and intestinal cancers. Moreover, obesity is the most common and costly nutritional problem in the United States.

The cause of many of these diseases is unknown. Such is the case with inflammatory bowel disease ("IBD"), the general term for diseases that cause inflammation in the intestines. For example, ulcerative colitis ("UC") is an IBD that causes inflammation of the mucosa lining of the large intestine. The inflammation usually occurs in the rectum and lower part of the colon, but it may affect the entire colon.

The most common symptoms of UC include abdominal pain, tenesmus, fecal urgency, and bloody diarrhea. A person with UC may also experience fatigue, weight loss, loss of appetite, rectal bleeding, and loss of body fluids and electrolytes. Although UC is generally not itself fatal, a more severe form of the disease may lead to the formation of toxic megacolon leading to bowel perforations or bowel obstruction. UC may also increase the risk of colon cancer depending on the duration, extent and severity of the disease.

Despite the prevalence of IBD, including UC and Crohn's disease, no theories regarding the cause have yet been proven. In fact, as stated in U.S. Patent No. 5,932,214, even the broader category of diseases known as IBD have "no cure, and exact causes of IBD are not yet understood." (Col. 1, lines 40-41). Yet, advances in UC have shown, however, that it is possible to control the inflammation without knowing the etiology of the disease. Present methods of treatment for UC depend upon the extent of the disease and the severity of the symptoms. To

distinguish the amount of colonic surface involved in the inflammation process, UC is divided into subgroups, including ulcerative proctitis, proctosigmoiditis, left sided UC and pancolitis. The locations of each of these subgroups of UC are illustrated in **Fig. 1**.

Present treatments for gastrointestinal disorders, in general, and for UC specifically, rely on drug therapy and, where such drug therapy is not effective, surgery is required. For example, initial treatment for mild to moderate UC may include the 5-ASA agents, including sulfasalazine, oral or rectal mesalamine, or olsalazine as well as conventional corticosteroid enemas. Another treatment for UC is disclosed in U.S. Patent No. 5,932,214. This method of treatment involves administration of an antibody, polypeptide or other molecule recognizing VLA-4 (very late antigen-4). Patients with persistent mild to moderate symptoms of active UC, in spite of these therapies (treatment - refractory), may require conventional corticosteroids orally. Patients with still persistent symptoms or those with severe UC may require immunosuppressive agents such as azathioprine or 6-MP. Cyclosporin may be considered for those who do not respond. If conventional treatment is successful, remission is usually maintained with sulfasalazine and/or oral or rectal mesalamine or olsalazine, and, in some cases with azathioprine/6-MP.

Crohn's disease like UC is an inflammatory disease of the intestinal tract, but unlike UC, may involve any part of the GI tract, from mouth to anus. The terminal ilcum is a common site of involvement in active Crohn's disease and may result in malabsorption syndromes. Symptoms include diarrhea, abdominal pain, nausea, weight loss, and growth retardation. Active disease may lead to intestinal obstruction, bleeding, fistula formation, rectal abscesses, bowel perforation and peritonitis, and increased susceptibility to bowel cancer.

Treatment of Crohn's disease involves use of 5-aminosalycilic acids, corticosteroids, and immunosuppressive drugs. Antibiotics are necessary for infections and surgery may be required for refractory Crohn's or the complications that may develop from the disease. 5-ASA compounds may cause headache, nausea, fatigue, abdominal pain, worsening diarrhea, and in some cases, hypersensitivity reactions leading to rash, fever hepatitis, pneumonitis, hemolytic anemia, and bone marrow suppression.

Long term use of corticosteroids may cause Cushing's Syndrome hyperglycemia, acne, muscle weakness, osteoporosis, and cataract formation, among other things. Immunosuppressive agents may cause hepatic toxicity, bone marrow suppression, and pancreatitis among other things. Response to therapy is measured by improvement in clinical signs/symptoms of the disease along with improvement in disease activity on gastrointestinal imaging, using endoscopy and barium x-ray studies.

With respect to infectious enteritis, there are a variety of viruses, bacteria, and parasites that can infect the digestive tract and cause sudden and sometimes violent symptoms, including nausea/vomiting, diarrhea (sometimes bloody), abdominal pain and cramping, fever, weakness, and loss of appetite. Among the viral causes, most are due to the *Rotaviruses* and the *enteric caliciviruses* such as *Norwalk virus*. Among the bacterial causes, *Salmonella*, *Shigella*, and *Camphylobacter* are the most common, but other pathogens like *pathogenic E. Coli*, *Vibrio* and *Yersinia* can occur in endemics both inside and outside the United States. Parasitic infection can be due to protozoal organisms like *Entamoeba histolytica*, *Giardia*, and *Cryptosporidium*.

Treatment of these infections include general supportive measures like bed rest, hydration, and nutritional support. Some require antibiotics or antiparasitic agents. These drugs can cause allergic reactions and can affect the normal bowel flora and cause superinfections with harmful bacteria like *Clostridium difficile*. Some may also effect other organ systems like the liver and kidneys. Clinical improvement can be monitored by the white blood count, and clearing of the offending pathogen on serial stool analysis.

Antimicrobial agents are responsible for 25% of drug induced diarrhea. The rates of antibiotic associated diarrhea ("AAD") vary from 5 to 39% depending on the specific type of antibiotic used. The mechanism of AAD may be due to functional disturbance of intestinal carbohydrate or bile acid metabolism, an allergic or toxic effect on the intestinal mucosa, a pharmacologic effect on motility, or a disruption of the normal intestinal flora causing an overgrowth of harmful bacteria like *Clostridium difficile*, *Clostridium perfinges*, *Staphylococcus aureus*, *Klebsiella oxytoca*, *Candida* species, or *Salmonella* species. About 10 to 20% of all cases of AAD are caused by *Clostridium difficile*, an anaerobic bacteria that secretes 2 enterotoxins, A and B, which can induce a severe colitis of the intestinal lining. Symptoms, at one end of the spectrum include a mild diarrhea, which resolves after discontinuation of the antibiotic, to severe disease causing high fever, leukocytosis, abdominal pain, profuse diarrhea, hypoalbuminemia, dehydration, and electrolyte disturbances. In rarer cases, toxic megacolon with perforation and death may occur.

The impact of AAD is reflected by higher medical costs, increased hospital stays, and increased rates of comorbidities. Treatment involves discontinuing the antibiotic, general

supportive measures, bed rest, hydration, electrolyte and nutritional support, and in some cases, treatment with other antibiotics like metronidazole and vancomycin, to help restore the normal balance of the intestinal flora. In the more severe cases, surgery and colectomy may be necessary. Parameters used to measure improvement include resolution of symptoms, restoration of fluid and electrolyte balance, normalization of the white blood count, and clearing of toxins on serial stool analysis. In some cases, endoscopic evaluation of mucosal damage is necessary.

Microscopic or lymphocytic colitis and collagenous colitis may represent variants of the same disease. The disease is characterized by a waxing and waning watery diarrhea that usually affects middle-aged females. Colonoscopy shows normal appearance of the mucosa but biopsy shows infiltration of the lamina propria with inflammatory cells and intraepithelial lymphocytes. It is only in collagenous colitis that a subepithelial band of collagen is present. The pathogenesis of the disorder remains a mystery but there is evidence, much like UC and Crohn's disease, that the inflammatory process may be triggered by a luminal agent. The disease is treated much like IBD with 5-ASA drugs and corticosteroid. 5-ASA products may cause headache, nausea, fatigue, abdominal pain and worsening diarrhea. Hypersensitivity reactions may lead to rash, fever, hepatitis, pneumonitis, hemolytic anemia, and bone marrow suppression. Long term use of corticosteroids may cause Cushing's disease, hyperglycemia, acne, muscle weakness, osteoporosis, and cataracts, among other things.

The majority of colorectal cancers, regardless of etiology, are believed to arise from adenomatous polyps. These polyps protrude from the mucosa and are visible endoscopically.

Regular lower GI screening and removal of polyps remains, by far, the best way to prevent colon cancer. Unfortunately, colon cancer still remains the second leading cause of cancer death in the U.S. primarily because of an unsatisfactory adherence to a regimented screening program. Certain hereditary syndromes (like Familial Polyposis) are characterized by the appearance of thousands of adenomatous polyps throughout the large bowel. If left surgically untreated, colorectal cancer will develop in almost all patients prior to age 40. To prevent colon cancer in these individuals, a total colectomy is usually required. There is currently no other hard and fast way to prevent colon polyps and thus colorectal cancer, but dietary factors, like enhancing fiber and lowering saturated fat intake, might help. Nonsteroidal anti-inflammatory drugs like sulindac and celecoxib hold some promise. Many times though, these nonsteroidal agents may produce adverse GI side effects, renal failure, edema, and hypertension.

Irritable bowel syndrome ("IBS") is the most common gastrointestinal disease in clinical practice, and although not life threatening, it causes great distress. The patient with IBS may present with one of 3 clinical variants: patients with spastic colitis complain primarily of chronic abdominal pain and constipation. A second group has chronic intermittent diarrhea, often without pain, and a third group has features of both and complain of alternating constipation and diarrhea. The cause of the disease is thought to be due to an altered intestinal motility and increased visceral perception leading to reflex intestinal motor activity. Significant psychologic disturbances may be seen in some patients with IBS. Depression, hysteria, and obsessive compulsive traits are common. Fiber supplements, tranquilizers, and anticholinergic agents are the mainstay of treatment. Unfortunately, no specific drug or dietary regimen affords good relief

in all patients, and, thus, a number of therapeutic maneuvers need to be tried. Response to treatment is based solely on relief of distressing symptoms. There are no laboratory studies used to monitor IBS.

Nonspecific diarrheal illnesses usually fall into one of five categories:

1.	Osmotic:	pancreatic insufficiency, bacterial overgrowth, celiac disease, lactase deficiency, Whipples disease, short bowel syndrome, abetalipoproteinemia;
2.	Secretory:	carcinoid syndrome, Zollinger Ellison syndrome, vasoactive intestinal peptide secreting pancreatic adenomas, medullary carcinoma of the thyroid, villus adenoma of the rectum;
3.	Inflammatory:	radiation induced colitis, eosinophilic gastroenteritis;
4.	Altered bowel motility:	neurogenic diseases;
5.	Facticious:	laxative abuse.

Treatment and monitoring vary according to the specific cause of the diarrhea.

Helicobacter pylori is a micro-aerophilic gram negative bacillus that invades the gastric mucosa inducing an inflammatory response in the epithelial cell layer causing an infiltration of polymorphonuclear leukocytes. It can cause gastritis that can lead to erosions and even ulceration of the stomach and duodenum. It is the most common cause of ulcer disease in the U.S. Eradication of this organism usually requires a proton pump inhibitor in combination with clarithromycin and either amoxicillin or metronidazole. For many patients, this combination is poorly tolerated and gastrointestinal side effects are common. Antibiotic associated diarrhea

along with hypersensitivity reactions can also occur. Eradication of *H. pylori* can be confirmed with either UGI endoscopy with biopsy and special staining for *H. pylori* or by the breath urea nitrogen test.

Hyperlipidemia is detected by finding an elevated cholesterol or triglyceride in fasting plasma. There are 6 types that have been described: I, IIa, IIb, III, IV, and V, and are distinguished by the pattern of lipoprotein elevation in plasma. Each type may be inherited or secondary to other disorders like diabetes mellitus or hypothyroidism. Left untreated, hyperlipidemia can lead to atherosclerotic vascular disease or in some cases acute pancreatitis. Treatment involves a low fat diet, exercise, restriction of alcohol, and lipid lowering drugs. The pharmacologic agents used include the "statins" (which may cause constipation, hepatitis, myositis, and GI disturbances), bile acid sequestrants (which may cause constipation, heartburn, nausea, and bloating), nicotinic acid (which may cause flushing, GI distress, or hyperuricemia), and fibrates (which may cause cholelithiasis, hepatitis, or myositis). Monitoring response usually involves checking fasting plasma LDL, HDL, and triglycerides levels.

Autoimmune disease are characterized by production of either antibodies that react with host tissue or immune effector T cells that are autoreactive to endogenous self peptides. Genetic factors likely play a role in the genesis toward auto antibody formation or in the case of Major Histcompatability Complex antigen association with autoimmune diseases via presentation of self or foreign peptides that stimulate inappropriate antiself response. Examples of autoimmune diseases include systemic lupus crythematosus, rheumatoid arthritis, and the vasculitis syndromes.

Treatment of these conditions usually include the use of corticosteroids and immunosuppressive agents. Long term use of corticosteroids may cause Cushing's syndrome, hyperglycemia, acne, muscle weakness, osteoporosis, cataracts, among other things. Immunosuppressive drugs may cause hepatic toxicity, bone marrow suppression, and pancreatitis, among other things. Monitoring of response is based on improvement in clinical signs/symptoms, improvement in parameters of inflammation like the westergren sedimentation rate and c reactive protein levels, and in some cases, reduction in blood levels of auto antibodies.

Obesity is the most common and costly nutritional problem in the U.S., affecting approximately 33% of adults. Kuezmarski RJ, Flegal KM, Campbell SM, Johnson CL. *Increasing Prevalence of Overweight Among US Adults.* JAMA 1994; 272:205-11. The underlying causes of obesity are complex and generally cannot be simplified to mere "overeating". Both physiological and psychological factors may be involved.

Unfortunately, the prevalence of obesity is on the rise, increasing by approximately 30% between 1980 and 1994. *Id.* Health care costs directly attributed to obesity amount to $68 billion per year, and an additional $30 billion per year is spent on weight reduction programs and special foods. *Long-Term Pharmacotherapy in the Management of Obesity: National Task Force on the Prevention and Treatment of Obesity.* JAMA 1996; 276-1907-15. Even so, treatment directed toward the long-term reduction of body weight is largely ineffective, and 90 to 95% of persons who lose weight subsequently regain it. Wadden TA. *Treatment of Obesity by Moderate and Severe Caloric Restriction: Results of Clinical Research Trials.* Ann Intern Med

1993; 229:688-93; Rosenbaum M, Leibel RL, *Pathophysiology of Childhood Obesity.* Adv Pediatr 1988; 35:73-137.

Obesity is associated with increased morbidity and mortality. It has been linked to a number of diseases including type 2 diabetes mellitus, hypertension, coronary artery disease, stroke, hypercholesterolemia, cholelithiasis, fatty liver disease, certain cancers (postmenopausal breast cancer and cancers of the colon, endometrium and kidney), musculoskeletal disorders (osteoarthritis), obstructive sleep apnea, and infertility, not to mention the social consequences and isolation that many patients with obesity experience. *Department of Agriculture, Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans*, 4th Ed. Home and Garden Bulletin No. 232. Washington, D.C.: Government Printing Office, 1995.

Current treatment strategies have been disappointing and largely ineffective for long-term success. Certainly every effort is made to set short-term goals and recognize the importance of lifestyle alterations in the form of increased exercise and decreased caloric intake. Drug therapy is now limited since fenfluramine and dexfenfluramine have been taken off the market due to their possible link to valvular heart disease. Two new agents, sibutramine (Meridia), a catecholaminergic and serotonergic agonist, and orlistat (Xenical), a lipase inhibitor, have recently been approved by the FDA. Unfortunately, sibutramine causes dry mouth, headaches, insomnia, constipation, and dose related increases in heart rate and blood pressure. *Sibutramine for Obesity.* The Medical Letter 1998; 40:32. Orlistat can cause flatulence, oily stools, and fecal urgency and interferes with the absorption of the fat soluble vitamins (A, D, E, and beta

carotene). *Orlistat for Obesity.* The Medical Letter 1999; 41:55-6. Both drugs are only indicated for short term treatment and weight gain after cessation is common.

Surgical therapy is reserved for patients with severe obesity or those with lesser obesity who have coexisting conditions. Jejunal-ileal shunting can be effective but is costly and frequently results in symptoms related to a blind loop. The more common gastroplasty procedure is also costly and can cause "dumping" associated with the passage of gastric contents into the intestine. These patients need to be followed carefully for intestinal obstruction and electrolyte disturbances. Excess consumption of liquid or semisolid foods can negate the benefits of both procedures. Browenll KD, Fairburn CG, eds. *Eating Disorders and Obesity: A Comprehensive Handbook.* New York: Guilford Press, 1995.

Generally, conventional treatment methods for most gastrointestinal disorders, autoimmune diseases and obesity are expensive for the patient. In addition, while the symptoms may be relieved by conventional treatments, there are known side effects resulting from conventional treatments. For example, the side effects associated with treatment of UC using 5-ASA agents include nausea, vomiting, heartburn, diarrhea, and headache. For immunosuppressive agents, side effects include pancreatitis, fever, rash, arthralgia, nausea, leukopenia, infection, and hepatitis. Side effects resulting from surgery relate to problems common to the use of any invasive procedure, QOL issues, and complications. Further, many current treatment methods do not appear to play a beneficial role, such as reduction in the risk of colon cancer.

Recently, a number of diseases are being treated by probiotics. The term "probiotic" implies use of bacteria which performs beneficial functions for the human organisms when they are present and alive in viable form.

Consider, for example, the composition of U.S. Patent No. 3,988,440 for treatment of gastritis, and for gastric and duodenal ulcers. This particular composition contains 4-5.5% lactic acid bacteria or, more specifically, *Lactobacillus bulgaricus*, which is cultivated in a soya media. Kawai, et al., U.S. Patent No. 4,710,379, discloses an agent that contains bacteria cells obtained from microorganisms belonging to the genius *Streptococcus*, but not the species *thermophilus*. Kawai, et al., also claims the method for stimulating growth of intestinal lactic acid flora by administering a microorganism belonging to the genius *Streptococcus* to a person recognized as being deficient in intestinal lactic acid bacteria.

Cavaliere Veseley, et al., U.S. Patent No. 5,716,615, discloses a method of treatment of gastrointestinal disorders and for treatment of hypercholesterolemia. The composition contains 10-95% of *Streptococcus thermophilus* and 90-5% *L. plantarum,* and *L. sasei*, and other bacteria (see Col. 2, line 30 - Col. 3, line 12). Cavaliere Veseley, et al., also suggests treatment for chronic hepatitis, high cholesterol, and irritable bowel syndrome with this composition.

Paul, U.S. Patent No. 5,531,988, discloses an invention which comprises a bacteria and whey-containing composition, which is a mixture of an immunoglobulin and a bacterium, such as *Lactobacilli* or *Bifidobacterium* or mixtures thereof. This composition is used to treat diarrhea, constipation, and gas/cramps.

Ford, U.S. Patent No. 5,636,202, discloses micro-encapsulated *Lactobacilli* bacteria orally administered to treat or present antibiotic associated or other chronic or acute diarrhea. Ford suggests use of *Lactobacillus bulgaricus*. Interestingly, the claims of Ford are directed only to treatment of skin infections.

Reddy, et al., U.S. Patent No. 6,080,401, discloses a medicinal preparation for treatment of a disease or disorder in humans and animals combining a drug in a dosage sufficient for effective treatment of a disease or disorder, and a viable probiotic in a quantity sufficient to increase the efficacy of the drug. Reddy discloses a combination of probiotics and herbal preparations for aiding in weight loss. The weight loss preparation includes probiotics having *Lactobacillus acidophilus* and *Bifidobacterium bifidus*.

Each of these probiotic treatments is limited in its application and effectiveness. It is desired to treat the aforementioned gastrointestinal and autoimmune diseases, hyperlipidemia and obesity in an effective and cost efficient manner using a single probiotic composition. Therefore, a new composition and method of treatment is needed that is effective in reducing symptoms, reasonable in cost to the patient, does not exhibit significant adverse side effects, and which may be beneficial in reducing the risk of colon cancer. Of course, it is also desirable that the composition be easy to manufacture and deliver to the patient.

SUMMARY

In accordance with the present invention, a probiotic composition and method for the treatment of obesity is provided that solves the deficiencies inherent in traditional treatments. The present invention provides an effective treatment for obesity that avoids adverse side effects,

is reasonable in cost for the patient, and may be beneficial in reducing the risk of obesity related diseases. Further, the present invention is relatively easy to manufacture and deliver to the patient.

In accordance with the present invention, a probiotic composition for the treatment of obesity is provided. The probiotic composition comprises a mixture having *Lactobacillus bulgaricus* and *Streptococcus thermophilus* lactic acid bacteria. The probiotic composition further comprises a carbohydrate enriched media whereby the mixture and media are combined and allowed to ferment until a desired ratio of the *Lactobacillus bulgaricus* and *Streptococcus thermophilus* organisms as well as a desired number of total organisms per gram are achieved. The desired ratio of *Lactobacillus bulgaricus* and *Streptococcus thermophilus* organisms ranges from about 1:1 to about 10:1. The desired number of *Lactobacillus bulgaricus* per gram ranges from about 3×10^8 to about 2×10^{11}. Once the desired ratios and number of organisms are achieved, the composition may be freeze dried.

The present invention further includes a method for treating obesity using the lyophilized probiotic composition. The method comprises the steps of providing a probiotic composition comprising a mixture of *Lactobacillus bulgaricus* and *Streptococcus thermophilus* lactic acid bacteria. The composition further comprises a carbohydrate enriched media where the mixture and the media are combined and allowed to ferment until a desired ratio of *Lactobacillus bulgaricus* and *Streptococcus thermophilus* organisms as well as a desired number of total organisms per dose (10 grams/dose) are achieved. Next, the lyophilized probiotic composition is administered to a patient.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows a diagrammatic view of the large intestines of a human indicating the locations of various subgroups of ulcerative colitis.

DETAILED DESCRIPTION

In accordance with the present invention, a probiotic composition for the treatment of obesity is provided. The probiotic composition comprises a mixture. The mixture comprises *Lactobacillus bulgaricus* and *Streptococcus thermophilus* lactic acid bacteria. The mixture may be in the form of a culture. The probiotic composition further includes a carbohydrate containing media whereby the mixture and media are combined and allowed to ferment until a desired ratio of the *Lactobacillus bulgaricus* and *Streptococcus thermophilus* organisms, as well as a desired number of total organisms and number of *Lactobacillus bulgaricus* per gram are achieved. The probiotic composition's desired ratio of *Lactobacillus bulgaricus* to *Streptococcus thermophilus* organisms range from 1:1 to about 10:1. Ratios of 1:1 to about 1:20 are also desirable as long as the number of *Lactobacillus bulgaricus* organisms per gram is between 3×10^8 to 1×10^{12}.

One particular embodiment of the present invention includes a desired ratio of *Lactobacillus bulgaricus* to *Streptococcus thermophilus* organisms of about 2:1 to about 9:1. Another embodiment of the present invention includes a desired ratio of *Lactobacillus bulgaricus* to *Streptococcus thermophilus* organisms of about 3:5. Yet another embodiment of

The present invention's desired number of total organisms per gram ranges from about 1 x 10^7 to about 2 x 10^{12} with the number of *Lactobacillus bulgaricus* organisms per gram ranging from about 3 x 10^8 to about 1x 10^{12}. One embodiment of the present invention includes the desired number of *Lactobacillus bulgaricus* per gram of about 5 x 10^9. Another embodiment of the present invention includes the desired number of *Lactobacillus bulgaricus* organisms per gram of about 1 x 10^7. Yet another embodiment of the present invention includes the desired number of *Lactobacillus bulgaricus* organisms per gram of about 2 x 10^{11}

The carbohydrate enriched media includes any such media as is common in the art. One embodiment of the present invention includes a carbohydrate enriched media that is a dairy product. Any dairy product may be appropriate, but milk is particularly useful as the media.

Upon achieving the desired ratios, the probiotic composition may be lyophilized and separated into specific dosing units. Note, "freeze dried" and "lyophilized" are used interchangedly herein. The dosing units may be packaged in one of several forms including but not limited to packets, capsules, tablets, or caplets. Any other packaging form as is common in the art may be utilized.

The present invention also includes a method for treating obesity using a probiotic composition of the present invention. The method comprises the steps of providing a probiotic composition, the probiotic composition comprising a mixture, the mixture comprising *Lactobacillus bulgaricus* and *Streptococcus thermophilus* lactic acid bacteria. The composition further comprises a carbohydrate enriched media whereby the mixture and media are combined and allowed to ferment until a desired ratio of the *Lactobacillus bulgaricus* and *Streptococcus*

further comprises a carbohydrate enriched media whereby the mixture and media are combined and allowed to ferment until a desired ratio of the *Lactobacillus bulgaricus* and *Streptococcus thermophilus* organisms, as well as a desired number of *Lactobacillus bulgaricus* organisms per dose are achieved. The resulting composition may be lyophilized and separated into dosing units. A typical dosing unit of the lyophilized composition comprises about 10 grams of the composition. The method further comprises administering the probiotic composition to a patient.

The method of the present invention further comprises selecting a dosing form of the probiotic composition and determining an initial dosing strength and initial dosing frequency. The effectiveness of the probiotic composition in treating the patient is also determined. Adjusting both the dosing strength and the dosing frequency may be required to effectuate positive results in the patient. The efficacy of the probiotic composition is determined by at least one option chosen from evaluating the improvement of the patient's clinical symptoms, or evaluating medically standard objective parameters as appropriate for a particular disorder. Such medically standard objective parameters include, but are not limited to, gastrointestinal imaging using, for example, endoscopy and barium x-ray studies, biopsy, histopathology, restoration of fluid and electrolyte balance, normalization of white blood count, serial stool analysis, checking fasting plasma LDL, HDL and triglycerides, and tracking physical properties such as weight, body measurements and Body Mass Index ("BMI").

The probiotic composition may be prepared by combining a starter culture in a carbohydrate enriched media. The starter culture comprises *Lactobacillus bulgaricus* and *Streptococcus thermophilus* lactic acid bacteria. The combination of starter culture and media is

allowed to ferment. During the fermenting process, temperature and pH of the combination is monitored and controlled as is well known in the art. The fermentation process is halted upon achieving a desired ratio of *Lactobacillus bulgaricus* to *Streptococcus thermophilus* organisms and a desired number of total organisms per gram/or the desired number of *Lactobacillus bulgaricus* per gram. The probiotic composition is concentrated after fermentation is complete and then lyophilized prior to packaging. After concentrating and lyophilizing, the probiotic composition can be packaged into desired dosing units. The lyophilized form dose comprises 10 grams of the composition. The packaged dosing units may be in any suitable form as is common in the art and can include, but not be limited to packets, capsules, caplets, or tablets.

One embodiment of the present invention has been used to successfully treat a 43 year old male resulting in significant weight loss. The lyophilized probiotic composition contained *Lactobacillus bulgaricus* and *Streptococcus thermophilus* in a ratio of 9:1 and totaling 5.4×10^9 organisms per gram and about 5×10^9 *Lactobacillus bulgaricus* bacteria per gram. It was found that the preparation when taken at a dose of 10 grams (5.4×10^{10} organisms/dose equals about 5×10^{10} *Lactobacillus bulgaricus*/dose) twice daily caused significant weight loss in a 43 year old male who had not experienced a similar success with diet and exercise alone. Over a 12 week period, records show a 17 pound weight loss and a drop in the calculated BMI from 28.4 to 26.1 (BMI equals weight in kilograms divided by the square of the height in meters). The individual was able to maintain this weight loss during 6 week follow-up despite an increase in caloric intake and without a change in physical activity or intercurrent illness.

Another embodiment of the present invention has been used to successfully maintain a significant weight loss in a 43 year old male. The lyophilized probiotic composition contained *Lactobacillus bulgaricus* and *Streptococcus thermophilus* in a ratio of 2:1 and totaling 5 x 10^8 *Lactobacillus bulgaricus* per gram. It was found that the preparation when taken at a dose of 10 grams twice daily maintained significant weight loss in a 43 year old male who had not experienced a similar success with diet and exercise alone. Over a 52 week period, records show the maintenance of a 17 pound weight loss and the calculated BMI of 26.1 (BMI equals weight in kilograms divided by the square of the height in meters). The individual was able to maintain this weight loss during the first 52 week follow-up of the original weight loss despite an increase in caloric intake and without a change in physical activity or intercurrent illness.

Yet another embodiment of the present invention has been used to successfully maintain a significant weight loss and BMI in a 43 year old male. The lyophilized probiotic composition contained *Lactobacillus bulgaricus* and *Streptococcus thermophilus* in a ratio of about 3:5 and totaling 2 x 10^{11} organisms per gram. It was found that the preparation when taken at a dose of 10 grams twice daily allowed the individual to maintain the 17 pound weight loss during a second 52 week follow-up to the original weight loss despite an increase in caloric intake and without a change in physical activity or intercurrent illness.

The exact mechanism for this observed response is not known. It is postulated that the metabolic activity of the two lactic acid bacteria vary according to the form in which they are delivered – in a freeze dried "fasting" state vs. a wet "fed state such as that seen in a cultured

yogurt. It is possible, therefore, that the freeze dried preparation is metabolically more active, and more active in fermenting carbohydrates in the upper gastrointestinal tract, thereby, rendering them unavailable to the host before absorption can take place in the small intestine. In this way, the carbohydrate load is lessened and a source of calories in the host's diet is eliminated. Thus, the present invention is a very safe and effective adjunct to diet and exercise in treating obesity and especially obese type 2 diabetics. Moreover, the method of the present invention can impact the comorbid illnesses linked to obesity, as previously discussed.

As can be readily seen, the present invention eliminates the deficiencies associated with traditional compositions and methods for treating obesity. The significant benefits of the present invention include effective treatment of the obesity, as well as an avoidance of traditional side effects associated with current treatments. Further, due in large part to the relatively simple manufacturing processes and inexpensive raw materials, the present invention is much less costly to the patient than traditional approaches to treatment of obesity. Although other advantages may be found and realized and various modifications may be suggested by those skilled in the art, it is understood that the present invention is not to be limited to the details given above, but rather may be modified within the scope of the appended claims.